Other

CRT-108

Electromechanical mapping to Determine Myocardial Viability in Reperfused and Nonreperfused Myocardial Infarction Models

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Aims: Similarly to patients presenting with acute coronary syndrome two kinds of animal models were evaluated by cardiac magnetic resonance imaging (cMRI) and electromechanical mapping (EMM). The balloon occlusion model characterizes the features of patients receiving reperfusion therapy, the coil deployment method imitated the features of "late comers", who did not receive any reperfusion therapy.
Methods and Results: Balloon occlusion in the left anterior descending coronary artery (LAD balloon group) or coil deployment in the LAD (LAD coil group) or circumflex artery (Cx coil group) were applied percutaneously to induce reperfused or non-reperfused myocardial infarction (MI) in sixteen domestic pigs. Regional left ventricular viability data were captured via cMRI and EMM. The unipolar voltage (UV) value was significantly ($p<0.05$) decreased in segments containing transmural and subendocardial late enhancement as compared with viable segments in the LAD balloon (7.64±0.33, 6.5±0.26, 5.39±0.32 mV), LAD coil (8.96±0.56, 6.97±0.46, 5.97±0.5 mV) and Cx coil groups (9.57±0.53, 6.06±0.61, 5.54±1.07 mV). Receiver operator characteristic analysis revealed area under the curve 0.809 and 0.691 in the LAD infarct territory and 0.864, 0.855 ($p<0.05$) in the Cx infarct territory for the UV compared to cMRI viability results as transmural late enhancement or viable tissue and subendocardial late enhancement or viable tissue, respectively.
Conclusion: Our study provides a comparison of baseline parameters in myocardial infarcts of different pathomechanism and location via non-invasive and invasive methods and emphasizes the application of both models in preclinical studies, especially if EMM is utilized for both diagnostic and therapeutic purposes.

Physiologic Lesion Assessment

CRT-109

Gender Disparities for Intravascular Ultrasound Minimal Lumen Area Cutoff for Optimal Correlation with Fractional Flow Reserve in Intermediate Lesions

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Background: Assessment of intermediate coronary lesions is still challenging. Fractional flow reserve (FFR) measurements of 0.8 or lower are considered clinically significant for physiological ischemia. Intravascular Ultrasound minimal lumen area (IVUS MLA) was suggested to correlate with FFR for the determination of significant Stenosis. This study aimed to examine gender differences for the IVUS MLA cutoff.
Methods: The FIRST trial is a multi-center, prospective, international registry of patients with intermediate coronary lesions defined as a stenosis of 40-80% by angiography. A total of 350 patients, 367 lesions were enrolled into the study at 10 sites in the United States and Europe. Patients were followed up to hospital discharge. The primary end point was a correlation between MLA and FFR and to identity a cut-off value for MLA corresponding to FFR of 0.8. This sub-analysis examines the differences and correlations between males and females, where there were 260 males and 90 females in the study population.
Results: A receiver operating characteristic curve (ROC) identified MLA <3.1 mm2 (sensitivity 64.1%, specificity 64.9%) as the best threshold value for FFR <0.8. The same analysis between men and women showed, the minimum lumen area (MLA) cut-off for males was 3.19 mm2 (sensitivity 63.8%, specificity 64.7%, r=0.315), and 2.57 mm2 (sensitivity 65.0%, specificity 72.2%, r=0.294) for females.
Conclusion: Anatomic measurements of intermediate coronary lesions obtained by IVUS show a moderate correlation to FFR values. The MLA cutoff for female is smaller when compared to Male. These findings are correlated to smaller vessel size in female and should be taken into account when IVUS MLA is used for assessment of severity of intermediate lesions.

Lesion Characteristics

	Overall (n=344)	Male (n=242)	Female (n=92)	P Value
LAD	190 (56.9%)	133 (55.0%)	57 (62.0%)	0.249
LCX	60 (18.0%)	44 (18.2%)	16 (17.4%)	0.866
RCA	80 (24.0%)	62 (25.6%)	18 (19.6%)	0.247
Proximal	110 (32.9%)	86 (35.5%)	24 (26.1%)	0.101
Mid	198 (59.3%)	141 (58.3%)	57 (62.0%)	0.540
Distal	19 (5.7%)	12 (5.0%)	7 (7.6%)	0.350
Pre RVD	2.97 ± 0.58	3.01 ± 0.59	2.87 ± 0.54	0.063

NURSE AND TECH ABSTRACTS

CRT-110

The Execution and Management of a Complex Clinical Trial

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By providing evidence for best practice, randomized clinical trials play a critical role in shaping the care of the public. We report the operational management systems that enabled the successful execution of a landmark randomized clinical trial. We propose a model for managing high-enrolling, multidisciplinary clinical trials. From 2007-2011 238 subjects were enrolled into TAVR Trial. All patients underwent robust screening assessment(Figure 1A)which was reviewed by our Heart Team at our weekly conference. The Heart Team incorporates expertise from multiple disciplines with subinvestigators from cardiac surgery, cardiology, anesthesiology, neurology. Both research and clinical studies were required during the following phases of care: screening, baseline, preoperative, intraoperative, postoperative,discharge,1month,6month,and every year thereafter out to 5 years (Figure 1B).A minimum of 2069 data points were captured to ensure compliance. Safety reporting required review of 969 adverse events of which 80% were significant, requiring review by the PI within 24 hours. Continual education and training of all team members was required due to protocol amendments (8 total). Protocol required specifics were necessary for all diagnostic studies. We screened >1000 patients. Rate of enrollment increased from 2 patients/month to 24-32 patients/month. Weekly heart team meetings facilitated contribution from all heart team members.THV clinic days were

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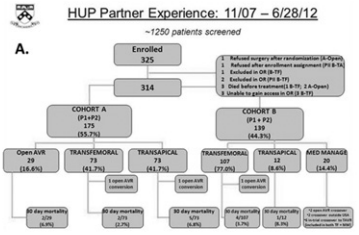
developed to streamline patient screening, study enrollment and ensure patient follow up. Patient care protocols and specific study instructions were developed and distributed to all healthcare providers. The TAVR research model proved to be a excellent platform for management of a complex clinical trial and was used as a template for the transition to a commercial TAVR program.



B.	Baseline	During procedure	Day 1	Discharge	30 Day	6 Month	12 Month	Annual Visit
Informed Consent	X							
History	X							
Physical Exam	X			X	X	X	X	X
NYHA Class	X			X	X	X	X	X
Adverse Event Assessment	X	X		X	X	X	X	X
Neurological Exams/Assessment	X			X	X	X	X	X
Risk Scoring	X							
Six Minute Walk Test	X				X	X	X	
Frailty Studies	X							
Laboratory Studies	X		X	X	X	X	X	X
Non-Invasive Tests	X		X	X	X	X	X	X
Invasive Tests	X	X				X		
Quality of Life Measures	X				X	X	X	X

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Angiomyogenesis, Cell Therapy, Gene Therapy

CRT-111

Hypoxia Reoxygenation-induced Myocardial Cell Apoptosis Can Be Rescued By Frizzled-2 Suppression

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Background: This study is aiming to find the signal transduction underlying calcium overloading caused cell apoptosis phenomenon post myocardial treatments.
Methods: For the information of Wnt5a/frizzled-2 signal pathway in mammalian cardiac cells were hardly seen before, first we needed to confirm the gene and protein expression of the effectors (wnt5a;frizzle-2;p-camkii, the marker presents the activation of this signal) which consisting this signal within myocardial cells, through q-rtpcr, western blot and some specific methods in detail.

Second, we transfected the cells with frizzled-2 gene in order to activate this pathway, and recorded the intracellular and cellular effects like cell apoptosis. Third, we used Stealth RNAi to conduct frizzled-2 gene suppression, then observed the following effects. Results indicated the role of Wnt5a/Frizzled-2 pathway played in calcium overloading process and cell apoptosis. Next, we analyzed the expression of the effectors of this pathway after the cells were conducted through hypoxia/reoxygenation treatment. In this part, the same testing objects and methods were used to consistent with different treatment groups.
Results: First, results from simple cell interference test showed that wnta5a, frizzled-2 and p-camkii is stable expressing in cardiac cells.

Second, High expression of p-CamkII followed by intracellular accumulation of calcium post frizzled-2 transfection indicates the activation of wnt5a/Frizzled-2 pathway. This was proved by gene suppression of frizzled-2 on the membrane: down regulation of frizzled-2 gene caused down expression of Frizzled-2 protein and p-CamkII marker, also the calcium accumulation and apoptosis.

Third, data from hypoxia/reoxygenation treatment group is found have the same trend echoes to part 1. Whatever in hypoxia group or in reoxygenation group, expression of Frizzled-2 on the cell membrane determines the character of wnt5a and downstream effectors, and eventually affects the intracellular calcium accumulation and apoptosis.
Conclusion: We hypothesis that activation of wnt5a/Frizzled-2 pathway post myocardial treatments could be a main reason causing calcium overloading and cell apoptosis. Results have proved our hypothesis, and this is the first paper in this area in evaluating this signal pathway within mammalian cardiac cells and raising a possible concept that activation of this signal pathway might be one of the mechanisms underlying cell apoptosis post myocardial treatments.

CRT-112

Exendin-4 Improves the Survival and Therapeutic Efficacy of Implanted Stem Cells Following Myocardial Infarction

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Background: The poor survival rate of stem cell transplantation in ischemic myocardial microenvironment is a major obstacle for stem cell therapy. Exendin-4 holds the potential of cardioprotective effect based on their pleiotropic activity. This study was designed to investigate whether the combination of Exendin-4 and adipose derived stem cells (ADSCs) could significantly improve the stem cells survival, engraftment and contribute to myocardial repair after myocardial infarction.
Material and Methods: The oxidative stress of cultured ADSCs was induced by H2O2 administration in vitro. The protective effect of Exendin-4 was investigated by dihydroethidium (DHE) staining and Live/Dead assay. For in vivo studies, MI was induced by the left anterior descending artery ligation in adult male Sprague-Dawley rats. ADSCs carrying dual-fusion (TF) reporter gene (fluc-mrfp) were quickly injected into border zone of myocardial infarction in rats treated with or without Exendin-4. PBS alone was injected as control. Multi-techniques were used to assess the beneficial effects after transplantation.
Results: The results showed that exendin-4 decreased ros level and reduced the necrosis of adscs suffered from oxidative stress significantly in vitro. one week after transplantation, inflammatory cells and oxidative stress of heart in exendin-4 group were decreased markedly than that in control group. four weeks after transplantation, the cardiac function evaluated by echocardiogram and MicroPET/ct improved significantly, while the infarct size and fibrotic area decreased significantly in Exendin-4+adscs group compared with that of other groups. both exendin-4 group and adscs group also improved myocardial performance. bioluminescence imaging showed exendin-4 promoted adscs survival significantly in vivo. histology examination showed that the combination of exendin-4 and adscs could reduce myocardial fibrosis, decrease myocardial apoptosis, increase vessel density, and enhance cardiogenic differentiation of adscs. western blotting demonstrated that oxidative stress and inflammation were significantly inhibited in the border area of infarction in Exendin-4+adscs group.
Conclusion: Through regulating the post-infarct microenvironment, exendin-4 combined with adscs can improve the survival and therapeutic efficacy of implanted stem cells. this study suggests the potential of exendin-4 for stem cell based heart regeneration.

Atherosclerosis

CRT-113

A Reproducible Animal Model of Calcified Atherosclerotic Plaque from a Cylindrical Bone Marrow Allograft Implanted in the Porcine Coronary and Peripheral Vasculature

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A reproducible animal model of calcified atherosclerotic plaque exhibiting properties similar to those observed in the human population has proven difficult to develop. We therefore investigated the use of a bone marrow plug, placed interventionally in the